

Supplemental Table 1: Sensitivity analyses to evaluate the impact of individual OBS components on the association between OBS and incident, sporadic colorectal adenoma

Model	OR (95% CI) [†]
Original model (reference)	0.93 (0.87 – 0.99)
OBS excluding PUFA, controlled for PUFA [‡]	0.94 (0.88 – 1.00)
PUFA 1 vs. 0 pts.	0.52 (0.28 – 0.97)
PUFA 2 vs. 0 pts.	0.55 (0.28 – 1.07)
OBS excluding serum ferritin, controlled for ferritin [‡]	0.92 (0.86 – 0.98)
Ferritin 1 vs. 0 pts.	1.04 (0.59 – 1.86)
Ferritin 2 vs. 0 pts.	0.95 (0.51 – 1.74)
OBS excluding vitamin C, controlled for vitamin C [‡]	0.92 (0.85 – 0.98)
Vitamin C 1 vs. 0 pts.	1.74 (0.95 – 3.17)
Vitamin C 2 vs. 0 pts.	1.38 (0.72 – 2.65)
OBS excluding plasma lycopene, controlled for lycopene [‡]	0.92 (0.86 – 0.98)
Lycopene 1 vs. 0 pts.	0.66 (0.37 – 1.19)
Lycopene 2 vs. 0 pts.	1.22 (0.66 – 2.25)
OBS excluding plasma α-carotene, controlled for α-carotene [‡]	0.94 (0.87 – 1.01)
α-carotene 1 vs. 0 pts.	0.67 (0.37 – 1.20)
α-carotene 2 vs. 0 pts.	0.85 (0.43 – 1.69)
OBS excluding plasma β-carotene, controlled for β-carotene [‡]	0.92 (0.85 – 0.99)
β-carotene 1 vs. 0 pts.	0.85 (0.47 – 1.54)
β-carotene 2 vs. 0 pts.	0.91 (0.46 – 1.82)
OBS excluding plasma lutein, controlled for lutein [‡]	0.91 (0.85 – 0.98)
Lutein 1 vs. 0 pts.	0.97 (0.54 – 1.74)
Lutein 2 vs. 0 pts.	1.56 (0.84 – 2.89)
OBS excluding plasma β-cryptoxanthin, controlled for β-cryptoxanthin [‡]	0.94 (0.87 – 1.01)
β-cryptoxanthin 1 vs. 0 pts.	0.99 (0.56 – 1.76)
β-cryptoxanthin 2 vs. 0 pts.	0.70 (0.37 – 1.32)
OBS excluding plasma α-tocopherol, controlled for α-tocopherol [‡]	0.91 (0.85 – 0.98)
α-tocopherol 1 vs. 0 pts.	1.78 (0.98 – 3.21)
α-tocopherol 2 vs. 0 pts.	1.55 (0.77 – 3.09)
OBS excluding selenium, controlled for selenium [‡]	0.92 (0.87 – 0.98)
Selenium 1 vs. 0 pts.	3.53 (0.28 –
Selenium 2 vs. 0 pts.	44.13)
OBS excluding smoking, controlled for smoking [‡]	1.63 (0.56 – 4.76)
Smoking 1 vs. 0 pts.	0.96 (0.89 – 1.02)
Smoking 2 vs. 0 pts.	0.63 (0.33 – 1.20)
OBS excluding aspirin, controlled for aspirin [‡]	0.40 (0.21 – 0.77)
Aspirin 1 vs. 0 pts.	0.93 (0.87 – 0.99)
Aspirin 2 vs. 0 pts.	N/A*
OBS excluding NSAID, controlled for NSAID [‡]	0.89 (0.54 – 1.48)
NSAID 1 vs. 0 pts.	0.94 (0.88 – 0.99)
NSAID 2 vs. 0 pts.	N/A*
OBS excluding alcohol, controlled for alcohol [‡]	0.72 (0.43 – 1.22)
Alcohol 1 vs. 0 pts.	0.94 (0.88 – 1.00)
Alcohol 2 vs. 0 pts.	1.39 (0.69 – 2.81)
	0.53 (0.28 – 0.99)

Abbreviations: OBS = oxidative balance score; OR = odds ratio; CI = confidence interval; PUFA = polyunsaturated fatty acid; Pts. = points; NSAID = non-steroidal anti-inflammatory drugs

[†]Odds ratios adjusted for age, race, sex, body mass index, family history of colorectal cancer in a first degree relative, hormone replacement therapy (among women), dietary fiber, physical activity, study (MAP I or MAP II), and the applicable individual OBS-excluded component

[‡]As continuous variable

* Results not available (N/A) due to small numbers (n=0 and n = 2 for aspirin and NSAID, respectively) in the 1-point category

Supplemental Table 2: Associations of the OBS (in quartiles) with incident, sporadic colorectal adenoma

OBS	Cases (n=139)*	Controls (n=201)*	OR (95% CI)†	p-trend
Quartile 1 (OBS 2 – 9)	44	43	1.0	0.04
Quartile 2 (OBS 10 – 13)	47	64	0.84 (0.46 – 1.56)	
Quartile 3 (OBS 14 – 16)	34	50	0.76 (0.38 – 1.51)	
Quartile 4 (OBS 17-24)	14	44	0.38 (0.17 – 0.88)	

Abbreviations: OBS = oxidative balance score; OR = odds ratio; CI = confidence interval

†Adjusted for age, race, sex, body mass index (BMI), total energy intake, plasma cholesterol, family history of colorectal cancer in a first degree relative, physical activity, hormone replacement therapy (among women), study (MAP I or MAP II).

*Total number of subjects in the model is lower due to missing covariate data.

Supplemental Table 3: Associations of the biomarkers (divided into quartiles) with incident, sporadic colorectal adenoma

Biomarker‡	Cases	Controls	OR (95% CI)†	p-value
FIP				
Quartile 1	23	37	1.0	0.14
Quartile 2	16	40	0.55 (0.24 – 1.27)	
Quartile 3	44	40	1.50 (0.72 – 3.12)	
Quartile 4	36	38	1.34 (0.60 – 3.02)	
FOP				
Quartile 1	25	50	1.0	0.02
Quartile 2	19	47	0.83 (0.39 – 1.75)	
Quartile 3	30	48	1.39 (0.69 – 2.80)	
Quartile 4	52	46	1.96 (1.00 – 3.83)	
CRP				
Quartile 1	22	49	1.0	0.07
Quartile 2	33	53	1.71 (0.84 – 3.50)	
Quartile 3	37	45	1.94 (0.93 – 4.06)	
Quartile 4	47	54	2.06 (0.98 – 4.30)	

Abbreviations: OBS = oxidative balance score; OR = odds ratio; CI = confidence interval; FIP = F₂-isoprostanes; FOP = fluorescent oxidation products; CRP = C-reactive protein

†Adjusted for age, race, sex, body mass index (BMI), total energy intake, plasma cholesterol, family history of colorectal cancer in a first degree relative, physical activity, hormone replacement therapy (among women), study (MAP I or MAP II).

*Total number of subjects in the model is lower due to missing covariate data.

‡Quartile based on study- and sex-specific median values among controls.

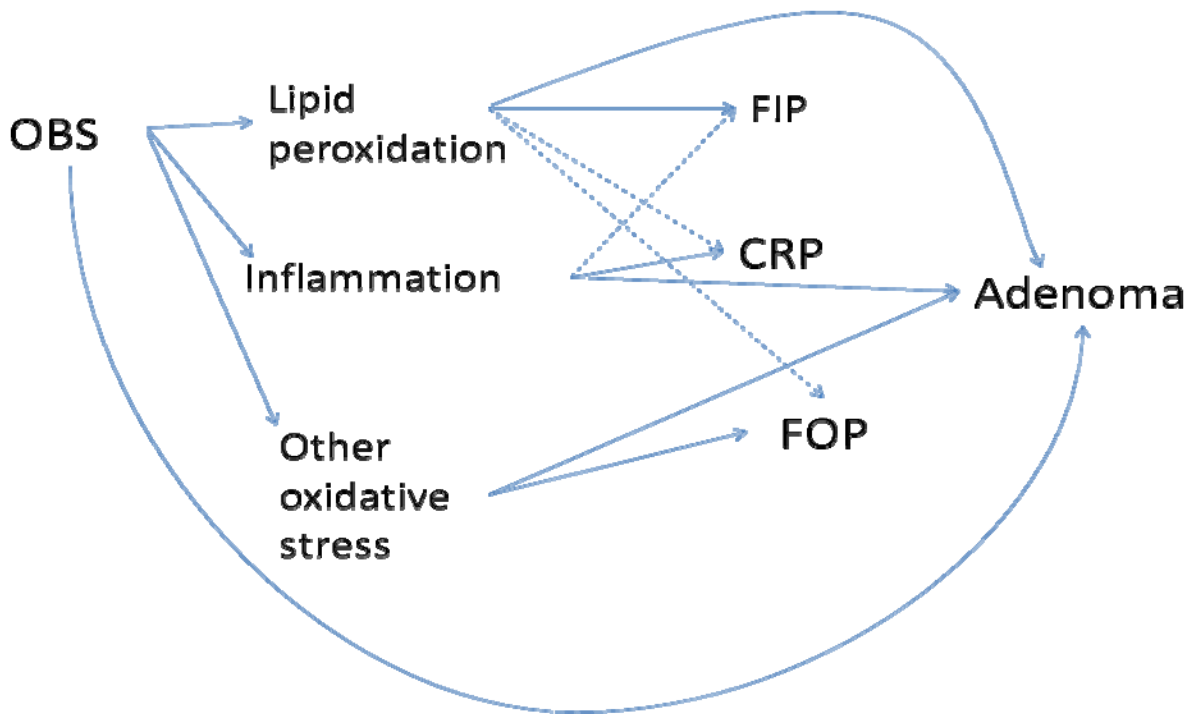
Supplemental Table 4. Association of individual OBS components with each biomarker

OBS Components	FIP		FOP		CRP	
	OR (95% CI) [†]		OR (95% CI) [†]		OR (95% CI) [†]	
	Male	Female	Male	Female	Male	Female
1. PUFA intake	1.15 (0.63 – 2.09)	1.35 (0.73 – 2.48)	1.01 (0.60 – 1.72)	0.88 (0.52 – 1.47)	0.73 (0.44 – 1.22)	0.68 (0.39 – 1.19)
2. Serum ferritin	1.13 (0.65 – 1.96)	1.00 (0.63 – 1.60)	1.25 (0.77 – 2.04)	0.91 (0.60 – 1.38)	0.83 (0.50 – 1.37)	0.96 (0.62 – 1.49)
3. Total vitamin C intake	0.52 (0.28 – 0.95)	0.66 (0.40 – 1.10)	1.11 (0.66 – 1.87)	1.09 (0.71 – 1.69)	0.60 (0.36 – 1.01)	0.66 (0.41 – 1.07)
4. Plasma lycopene	0.93 (0.55 – 1.57)	1.08 (0.65 – 1.79)	2.33 (1.40 – 3.88)	3.48 (2.10 – 5.77)	1.17 (0.73 – 1.88)	1.39 (0.88 – 2.21)
5. Plasma α-carotene	0.90 (0.50 – 1.64)	0.82 (0.50 – 1.35)	2.06 (1.19 – 3.54)	1.77 (1.11 – 2.84)	0.74 (0.45 – 1.23)	0.49 (0.30 – 0.81)
6. Plasma β-carotene	0.81 (0.47 – 1.41)	0.61 (0.37 – 1.00)	2.32 (1.34 – 4.02)	1.42 (0.93 – 2.19)	0.67 (0.41 – 1.11)	0.54 (0.33 – 0.86)
7. Plasma lutein	0.98 (0.57 – 1.67)	0.69 (0.43 – 1.09)	1.42 (0.86 – 2.35)	1.34 (0.88 – 2.02)	0.92 (0.57 – 1.49)	0.73 (0.47 – 1.15)
8. Plasma β-cryptoxanthin	0.70 (0.40 – 1.24)	0.76 (0.48 – 1.20)	1.33 (0.81 – 2.17)	1.15 (0.77 – 1.72)	0.69 (0.42 – 1.13)	0.60 (0.39 – 0.93)
9. Plasma α-tocopherol	0.59 (0.31 – 1.09)	0.46 (0.26 – 0.82)	1.45 (0.86 – 2.43)	1.04 (0.64 – 1.70)	1.04 (0.62 – 1.76)	0.72 (0.43 – 1.21)
10. Selenium supplements	0.62 (0.23 – 1.63)	0.80 (0.35 – 1.82)	0.52 (0.23 – 1.17)	1.31 (0.64 – 2.65)	0.31 (0.09 – 1.06)	1.38 (0.64 – 2.95)
11. Smoking history	0.35 (0.18 – 0.69)	0.75 (0.46 – 1.22)	0.71 (0.41 – 1.21)	0.59 (0.39 – 0.90)	0.55 (0.32 – 0.95)	0.88 (0.57 – 1.36)
12. Regular aspirin use	0.82 (0.51 – 1.33)	0.97 (0.63 – 1.49)	1.01 (0.67 – 1.54)	1.09 (0.76 – 1.55)	0.76 (0.49 – 1.17)	0.79 (0.54 – 1.15)
13. Regular NSAID use	0.60 (0.33 – 1.07)	0.99 (0.67 – 1.48)	0.86 (0.54 – 1.36)	0.98 (0.71 – 1.40)	0.93 (0.57 – 1.50)	1.08 (0.76 – 1.54)
14. Alcohol consumption	0.77 (0.47 – 1.26)	0.75 (0.44 – 1.30)	0.68 (0.43 – 1.09)	0.95 (0.59 – 1.51)	0.90 (0.58 – 1.41)	1.07 (0.66 – 1.75)

Abbreviations: OBS = Oxidative Balance Score; PUFA = Polyunsaturated fatty acid; NSAID = Non-steroidal anti-inflammatory drug; FIP = F₂-isoprostanes; FOP = fluorescent oxidation products; CRP = C-reactive protein

[†]Adjusted for age, race, sex, body mass index (BMI), total energy intake, plasma cholesterol, and family history of colorectal cancer in a first degree relative, and hormone replacement therapy (among women), fiber, physical activity, and study (MAP I or MAP II).

Supplemental Figure 1



A hypothetical directed acyclic graph (DAG) showing possible inter-relationship of OBS, biomarkers of oxidative stress (FIP and FOP) and inflammation (CRP), and colorectal adenoma. We first assume that OBS affects three main processes: lipid peroxidation (a component of oxidative stress), inflammation, and some other oxidative stress-related process that is independent of lipid peroxidation. Second, we also assume that each component affects the level of a biomarker: lipid peroxidation is mainly associated with FIP, inflammation with CRP, and non-lipid peroxidation components of oxidative stress with FOP (dotted arrows are weak effects). All effects are positive, except where indicated by a “-” sign.

Abbreviations: FIP = F₂-isoprostanes, FOP = fluorescent oxidation products, CRP= C-reactive protein.